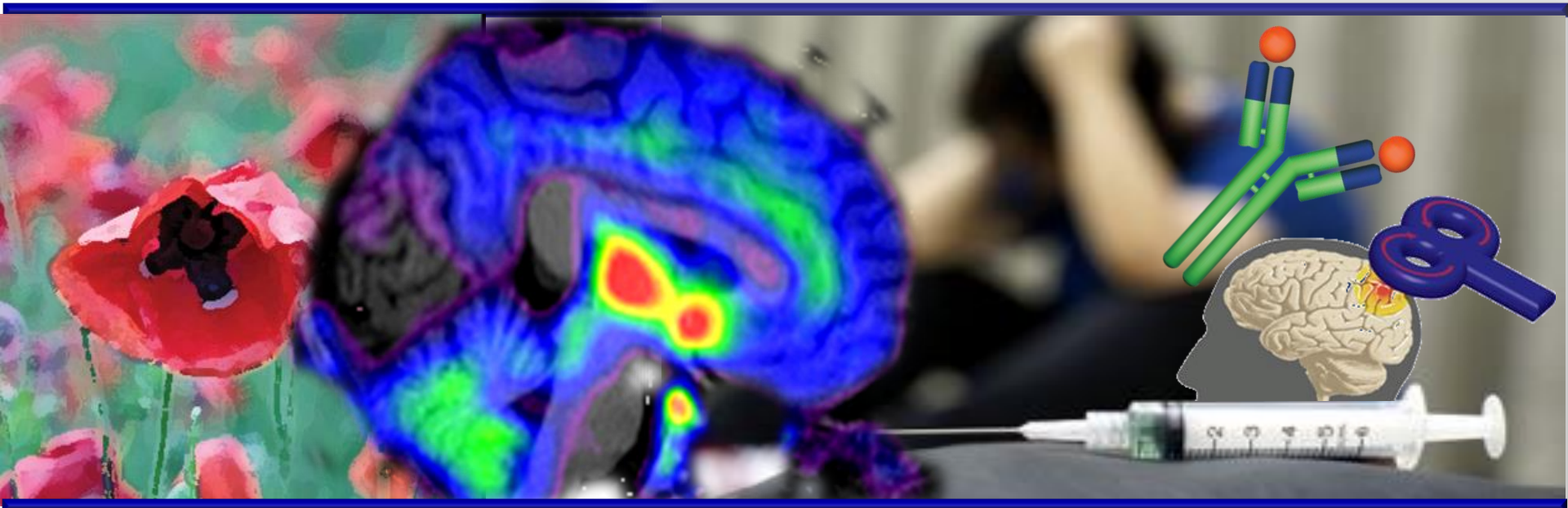


OPIOID UPDATE



Nora D. Volkow, M.D.
Director



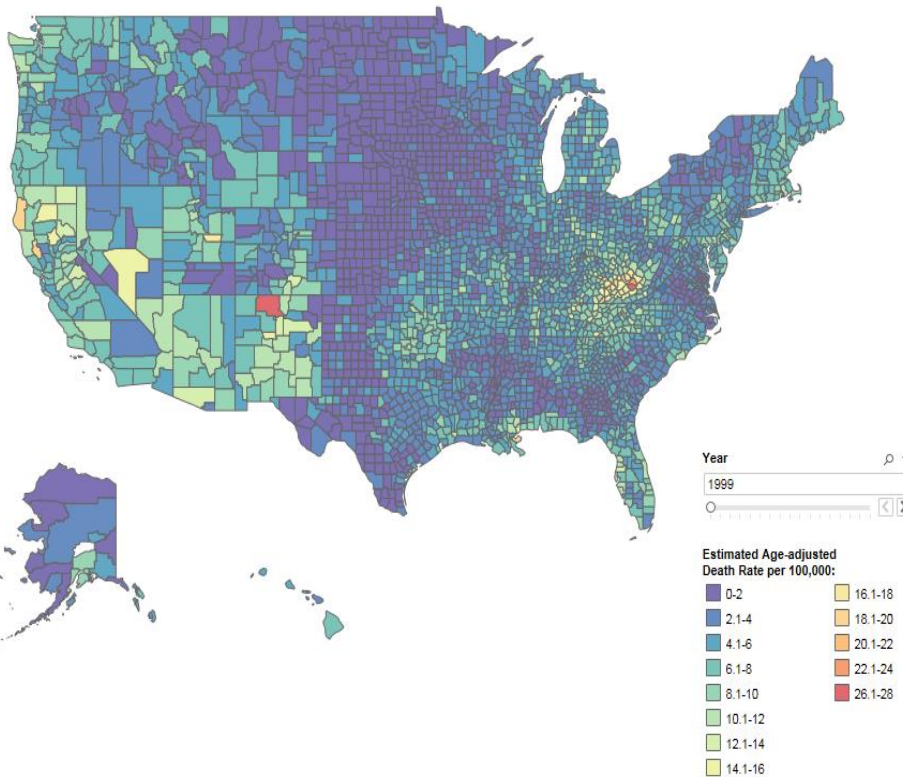
National Institute
on Drug Abuse



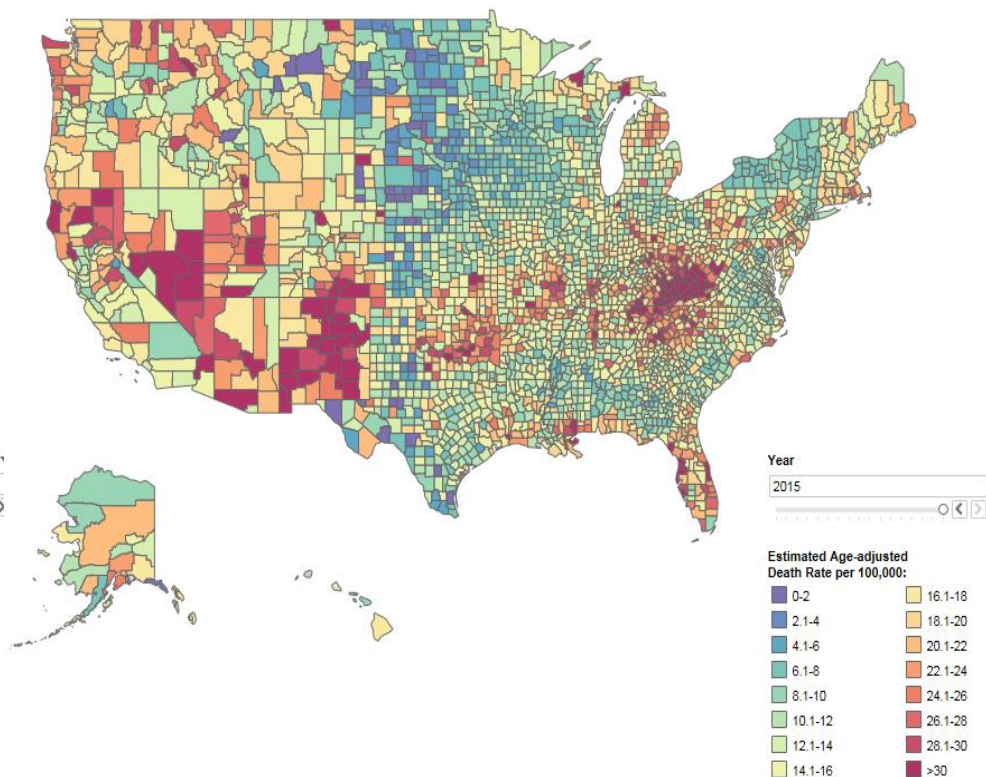
@NIDAnews

Overdose Death Rates

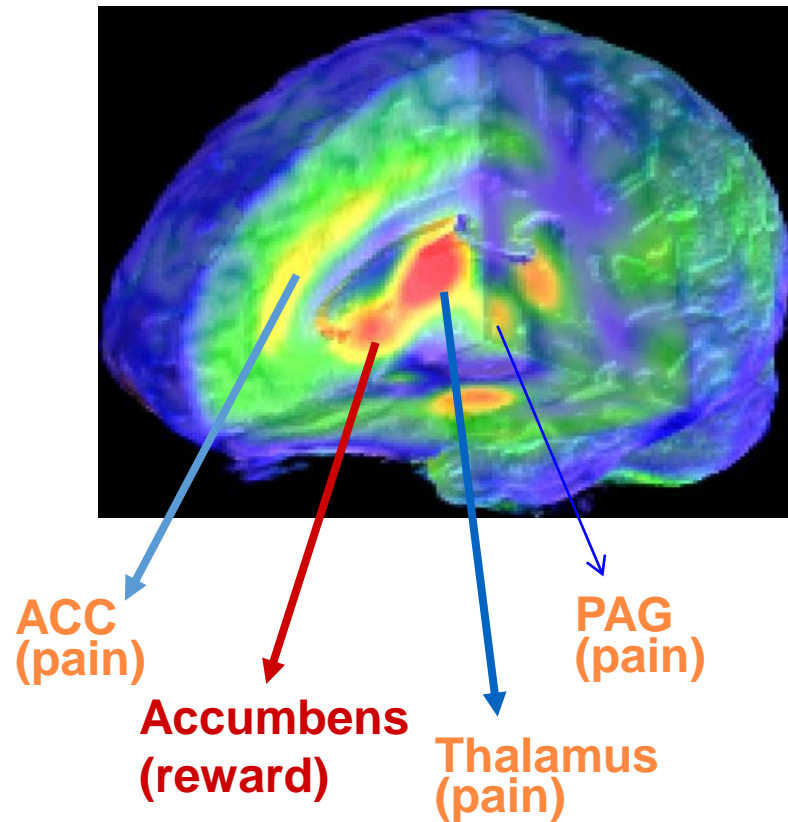
1999



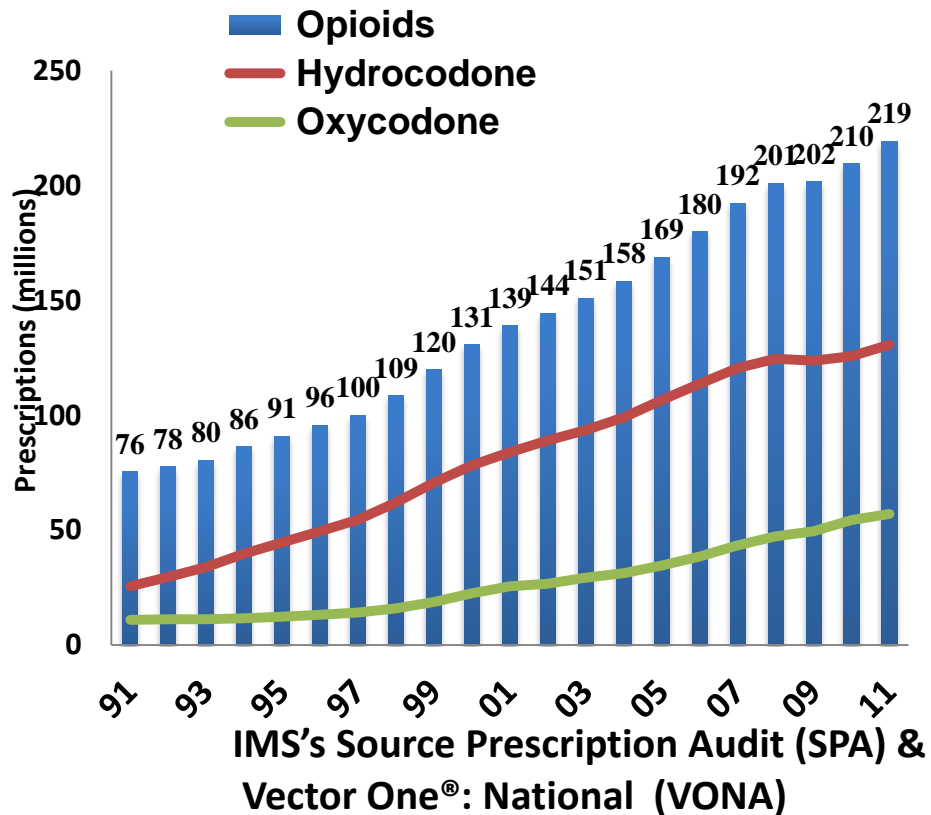
2015



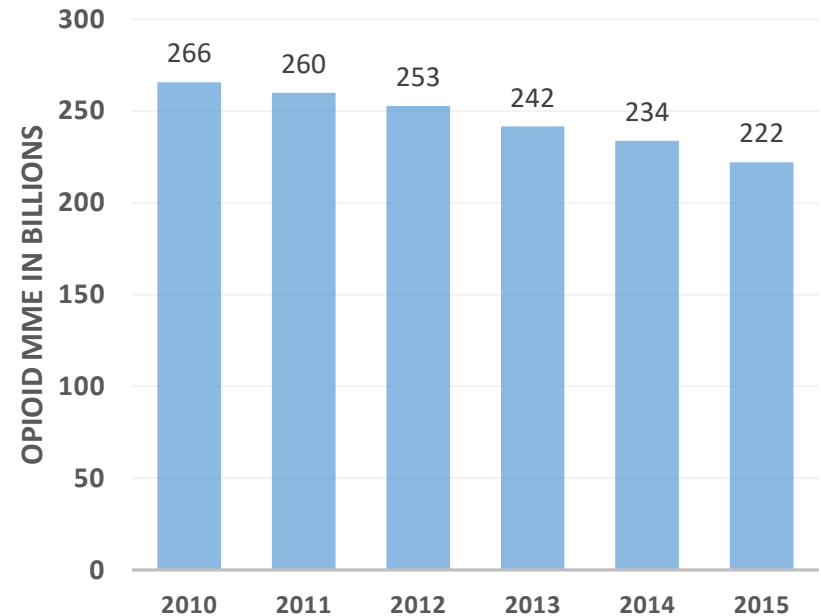
Analgesic Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)



Opioid Prescriptions 1991-2011

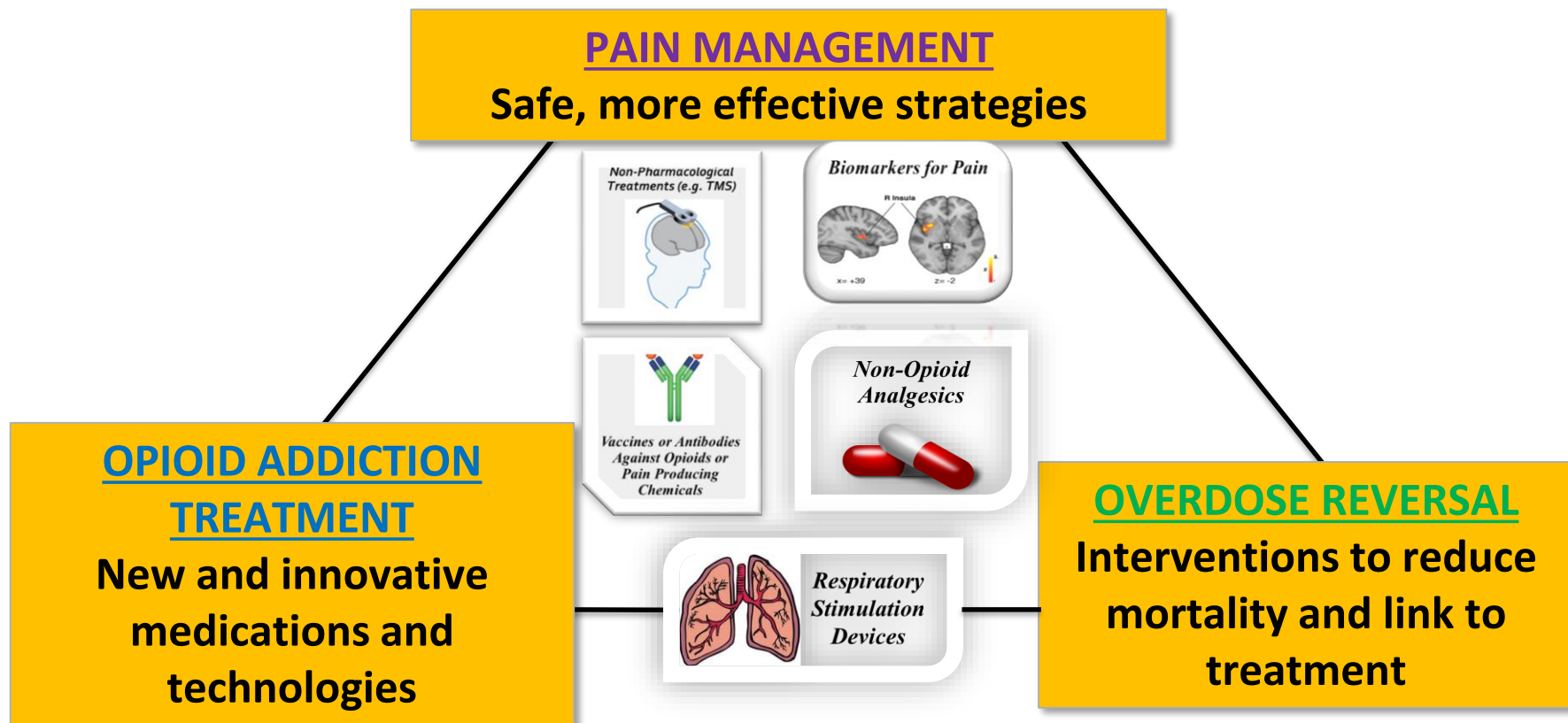


Opioid morphine milligram
equivalents (MME)
dispensed fell >15% from
2010-2015

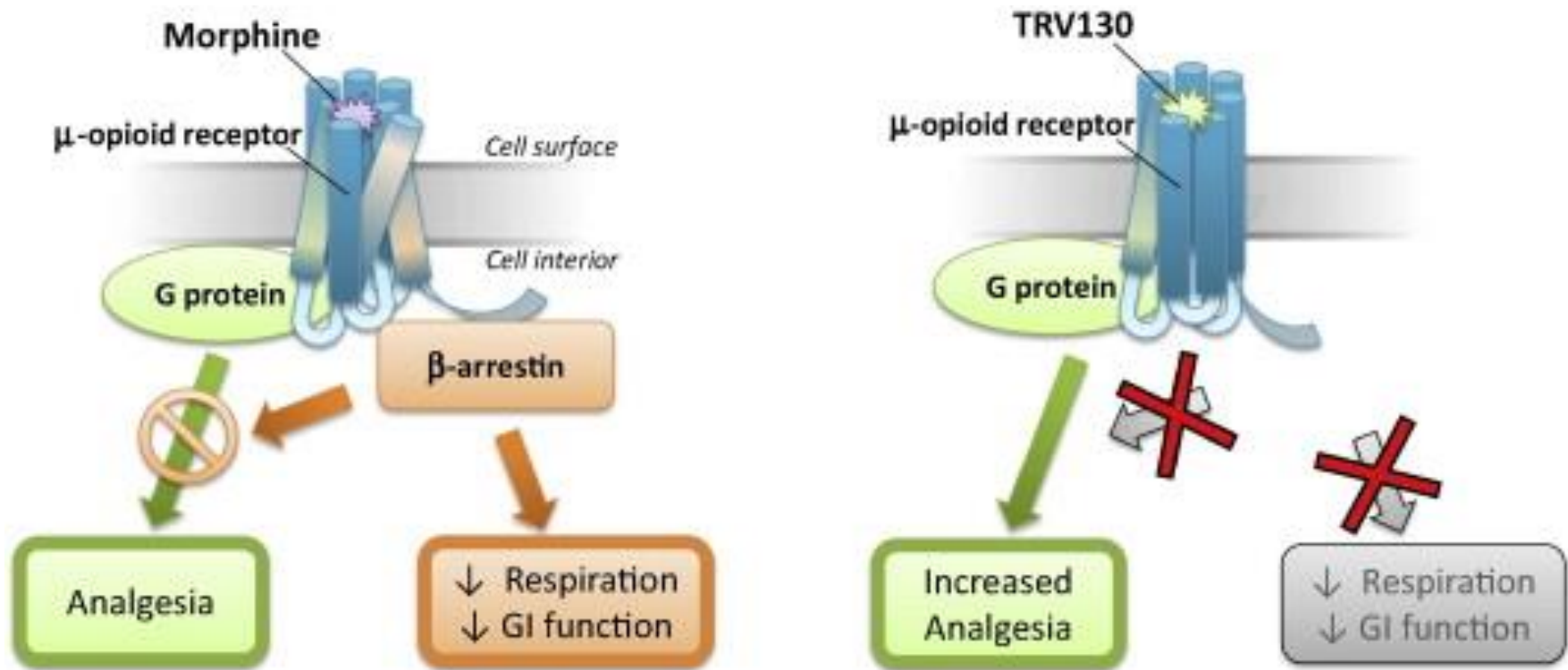


NIH OPIOID RESEARCH INITIATIVE

Using Research to End the Opioid Crisis



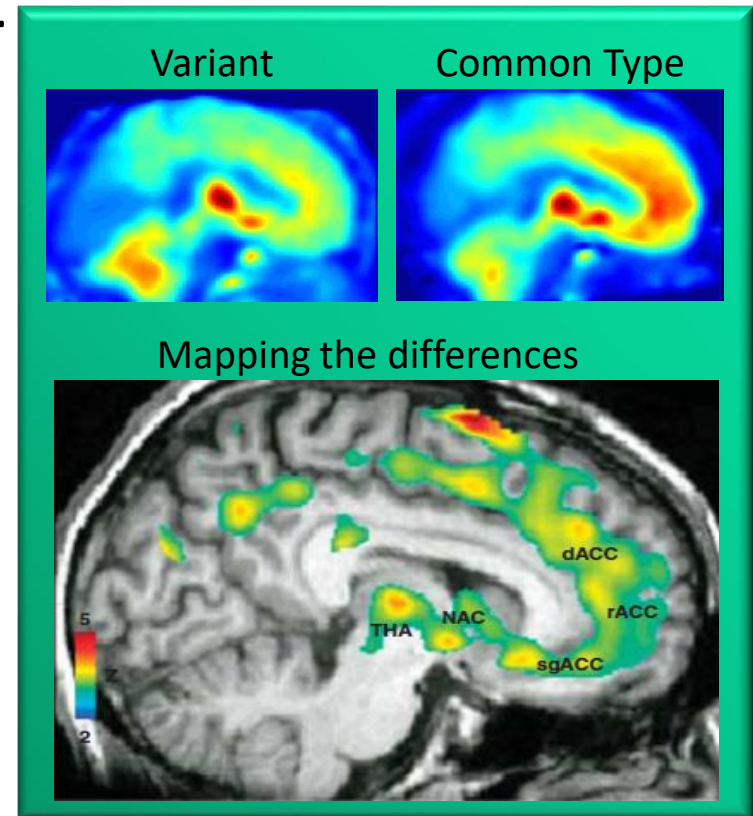
Biased Mu-Opioid Receptor Ligands: A Promising New Generation Of Pain Therapeutics



Biomarkers for Personalized Treatment

Imaging + Genetics → Addiction Prediction

- ***OPRM1*** encodes for target of opioids – and varies from person to person
 - Can variants predict likelihood of addiction?
- ***OPRM1*** variant
 - Affects specific receptor levels in brain
 - Associated with increased risk for addiction, overdose severity
- Highlights *precise, personalized* nature of addiction....



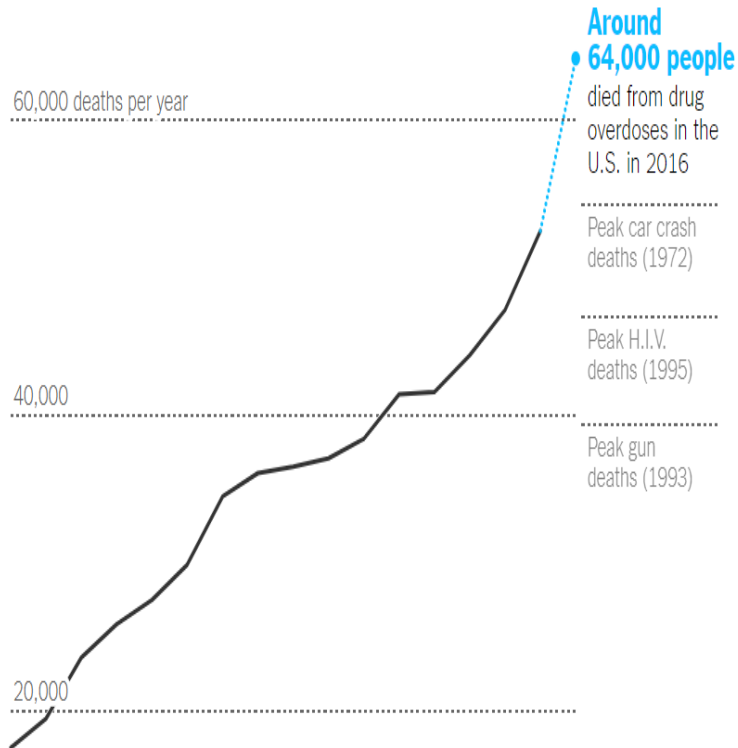
Peciña et al., *Neuropsychopharmacology* 2015; 40

Hancock et al., *Biol Psychiatry* 2015; 78

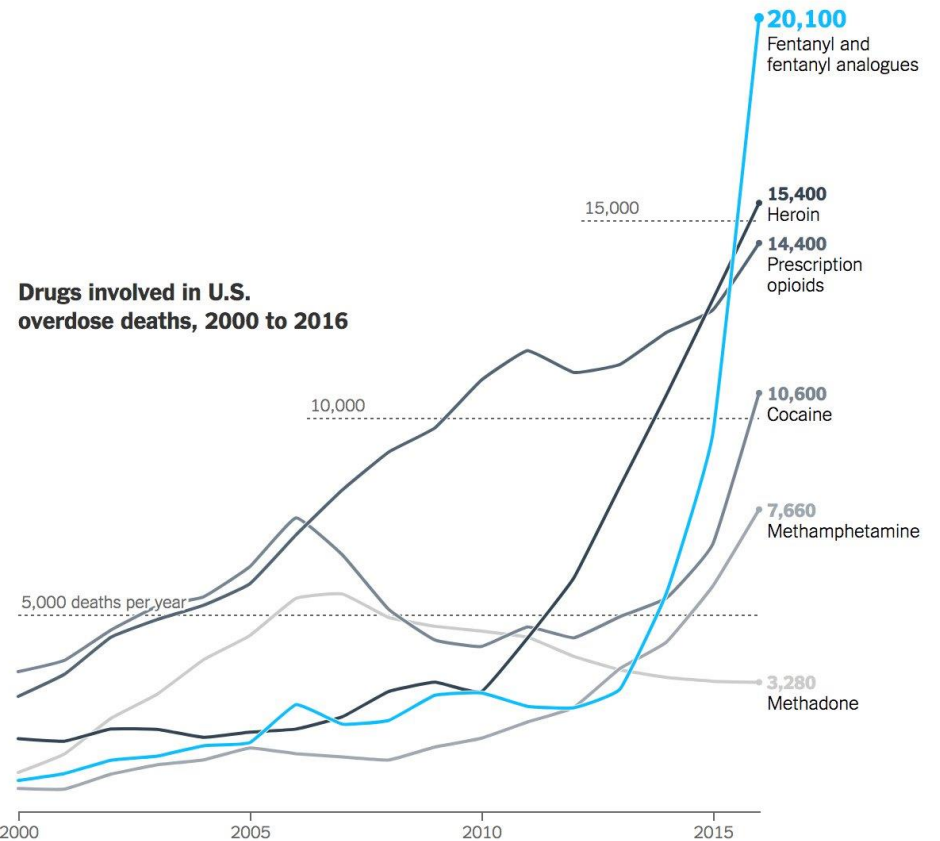
Manini et al., *J Med Toxicol* 2013; 9

Estimate of Total U.S. Drug Deaths in 2016

Total U.S. drug deaths



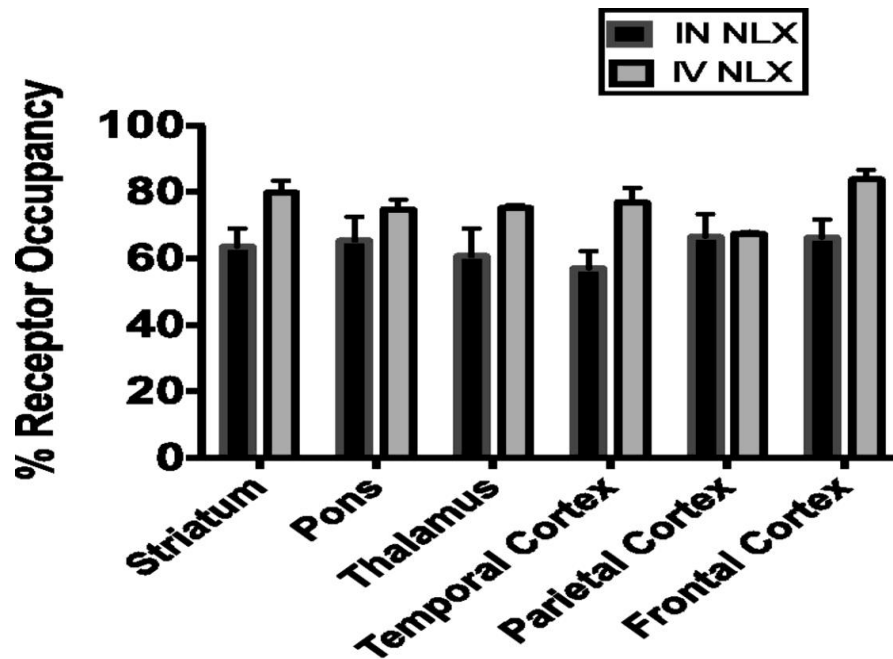
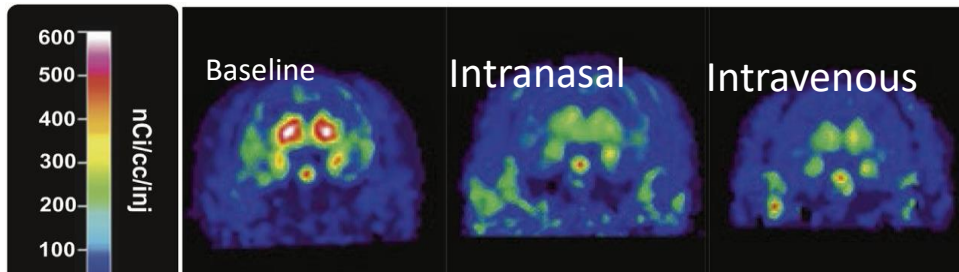
Fentanyl-Related Deaths Surpassed Heroin or Rx Opioids in 2016



Graphs from [NY Times Article](#) based on [CDC MMWR Report 2017](#)

NALOXONE REQUIRES FAST AND EFFICIENT DELIVERY as achieved with iv injection but few know how to inject

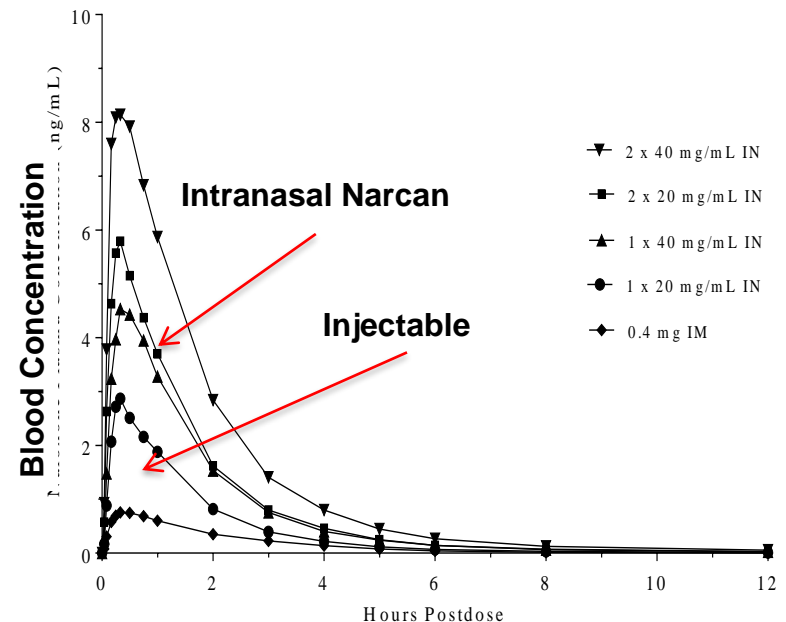
Receptor occupancy by INTRANASAL
equivalent to INTRAVENOUS Naloxone



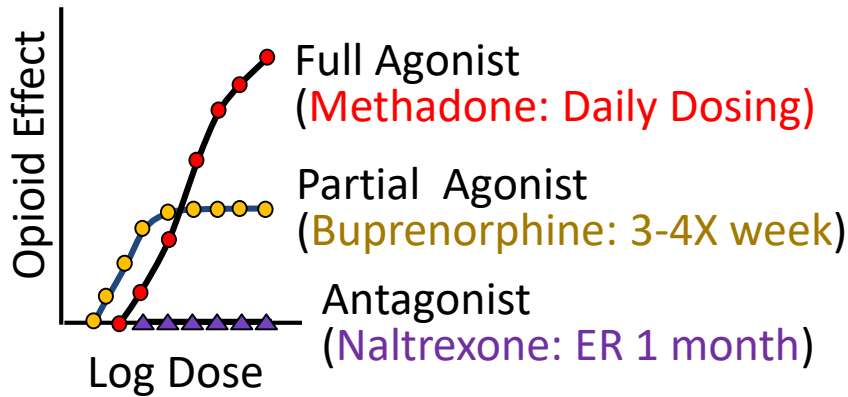
Phillip et al. J Pharmacol Exp Ther 2016



Intranasal naloxone reaches blood
as fast as Intramuscular naloxone
and achieves higher levels



Medication Assisted Treatment (MAT)



DECREASES:

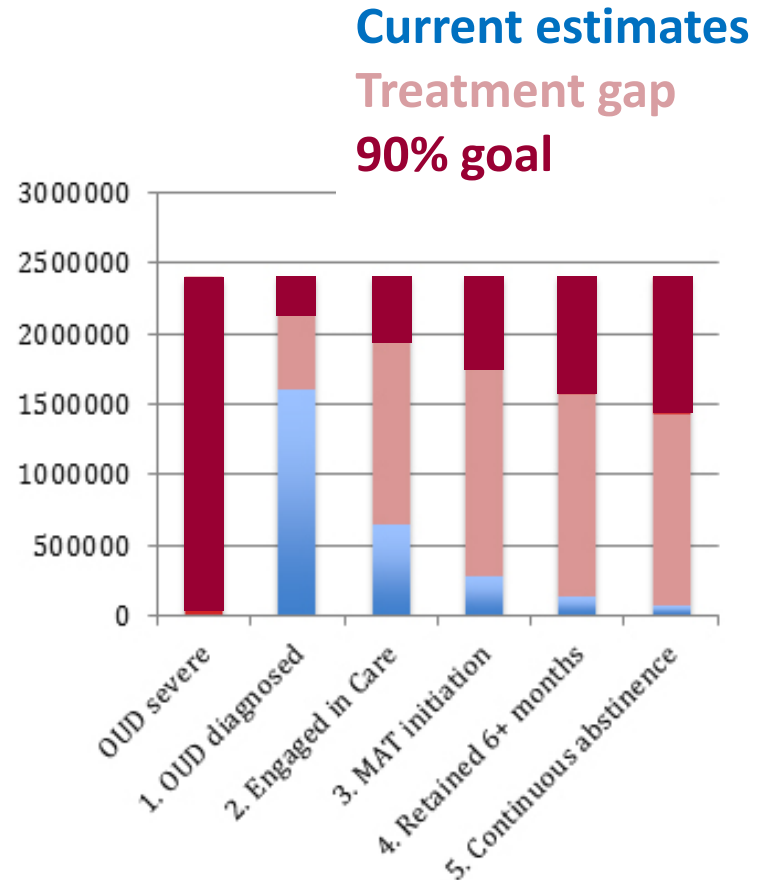
- Opioid use
- Opioid-related overdose deaths
- Criminal activity
- Infectious disease transmission

INCREASES

- Social functioning
- Retention in treatment

But MAT is highly underutilized!
Relapse rates are very high!

OUD Cascade of Care in USA



*Williams AR, Nunes E, Olfson M.
Health Affairs Blog, 2017*

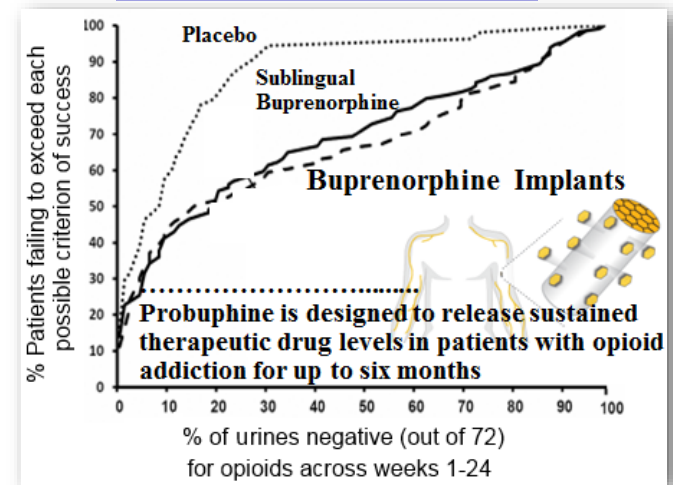
New and Innovative Opioid Addiction Treatments

- Improved opioid based medications
- New non-opioid based medications
- Biologics (e.g., vaccines, antibodies)
- Non-pharmacological treatments

Extended Release Medications Improve Compliance



Probuphine

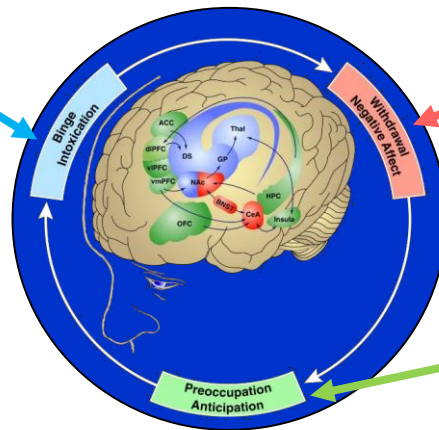


Rosenthal et al., Addiction 2013;105.

FDA approval – May 26, 2016

Target Selection on the Basis of the Neurocircuitry of Addiction

Targets to interfere with drug reward



Targets to reduce stress-induced drug seeking and to improve mood

Targets to reduce cue-induced drug seeking and to improve executive function

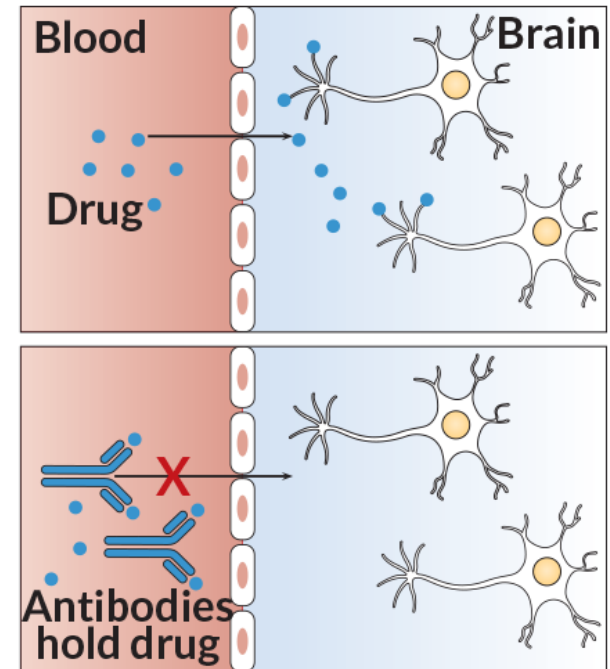
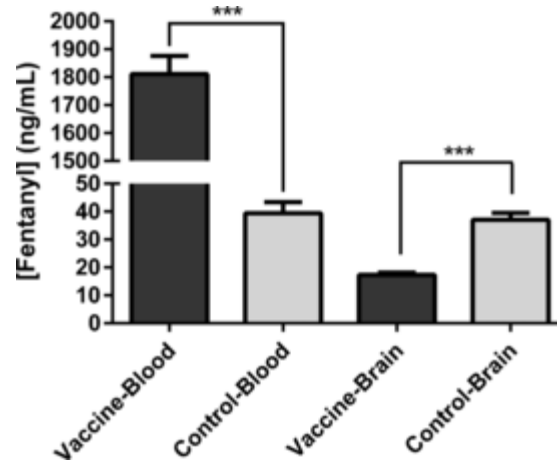
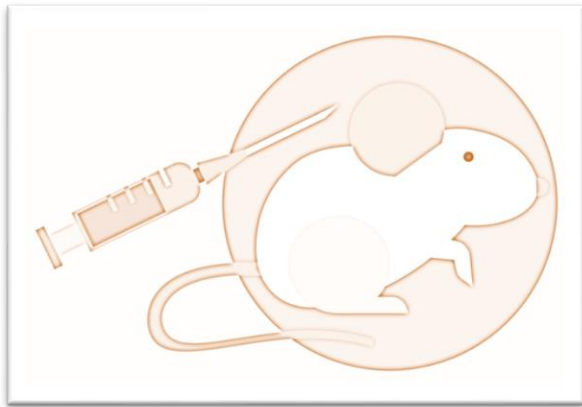
*Diagram: Koob GF, Volkow ND.
Neuropsychopharmacol Rev, 2010*

Compounds targeted to neurocircuitry could be beneficial not just to addiction but also to diseases for which such circuits are disrupted (ie ADHD, depression)

Innovative Opioid Addiction Treatments – Fentanyl Vaccine

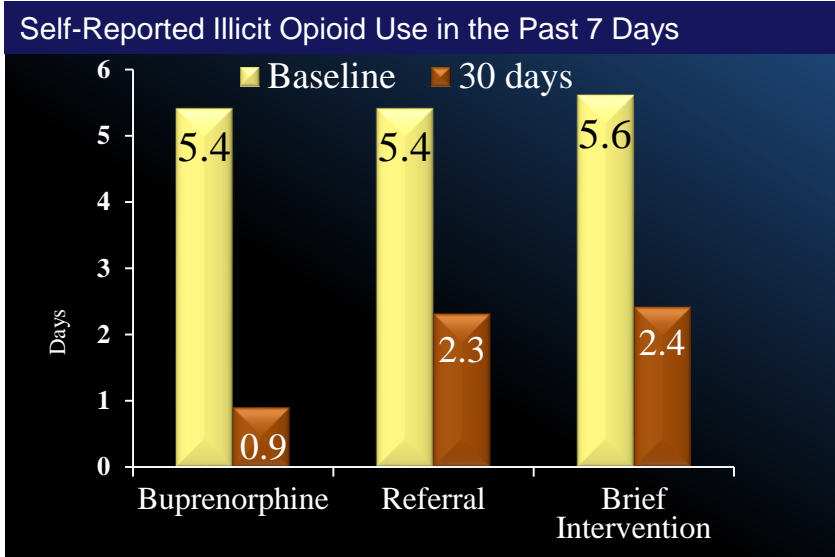
2016: First vaccine for fentanyl and fentanyl analogs reported in a mouse model

- Successfully stimulated antibody production
- Reduced fentanyl reaching the brain
- Reduced analgesia and protected against overdose



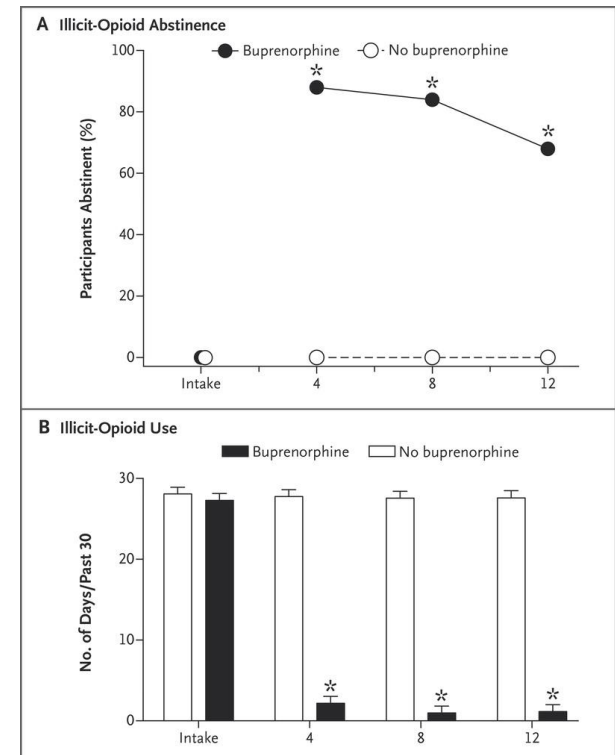
Emergency Department-Initiated Buprenorphine

- Reduced self-reported, illicit opioid use
- Increased engagement in addiction treatment
- Decreased use of inpatient addiction treatment services



D'Onofrio G et al., JAMA April 28, 2015.

Abstinence from Illicit Opioids over 12 Weeks with Interim Buprenorphine

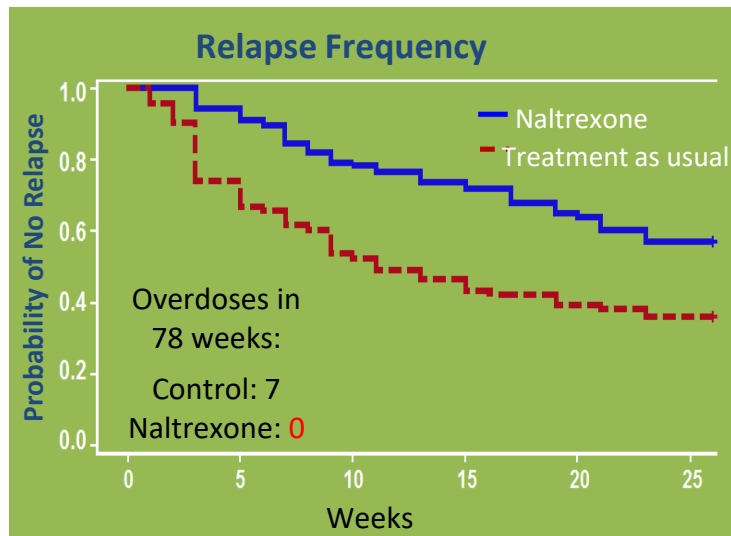


Sigmon SC et al. N Engl J Med 2016.

Treatments in Criminal Justice: Use of ER naltrexone

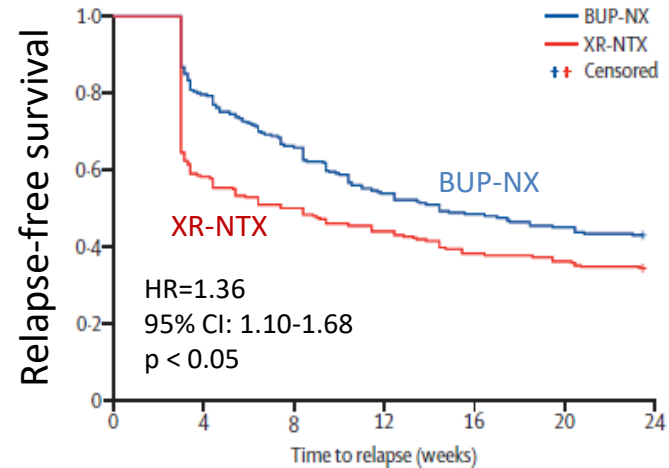


- *Participants:* parolees/probationers with opioid addiction received either
 - Monthly ER naltrexone for 6 months
 - Community treatment, including methadone or Suboxone (encouraged)

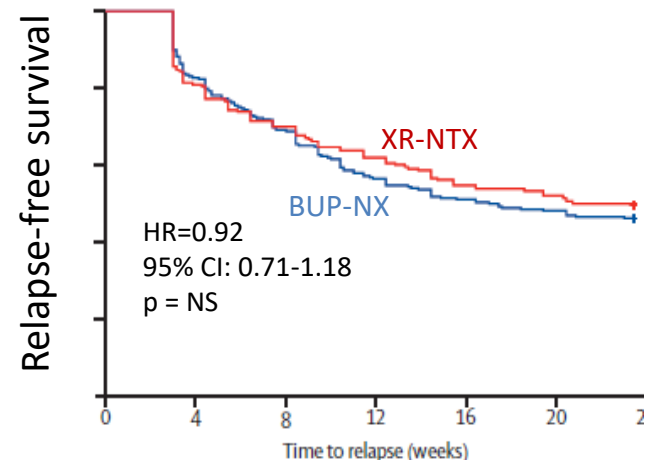


Comparative Effectiveness: Bup-NX vs ER Naltrexone

Intent-to-Treat Sample (n=570)



Per-Protocol Sample (n=474)



NIH Public Private Partnership to Address Opioid Crisis

Focus Area A:

Enhance the range of medication options to treat opioid use disorder and prevent/reverse overdoses.

- Develop new formulations and combinations of medications to treat opioid use disorder and to prevent overdoses
- Develop more potent or longer lasting opioid antagonists to reverse overdoses from fentanyl or its derivatives.
- Develop and validate alternative endpoint other than abstinence that are acceptable to FDA for approval of OUD medications

NIH Public Private Partnership to Address Opioid Crisis

Focus Area B: Pain

- Establish data sharing collaborative between industry groups
 - NIH to serve as a neutral broker
- Determine objective measures to understand, predict responses to pain
 - Biomarkers for pain – and a “Pain-ometer”
- Clinical trial network to accelerate trials on common and rare pain syndromes and to evaluate biomarkers